Effects of Trisomic Dyrk1a and EGCG Treatment on Craniofacial Development in Ts65Dn Down Syndrome Mice

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Down syndrome (DS), also known as Trisomy 21, is a genetic disorder caused by an extra copy of human chromosome 21. Individuals with DS exhibit various phenotypes such as cognitive, skeletal and craniofacial abnormalities. The Ts65Dn mouse model displays similar craniofacial abnormalities as observed in humans with DS including a small, undersized mandible. To gain a better understanding of craniofacial abnormalities, we study the molecular and cellular mechanisms underlying these abnormalities. Previous studies conducted in our lab identified a deficit in neural crest (NC) cells in the first pharyngeal arch (PA1) or mandibular precursor by embryonic day 9.5 (E9.5). We hypothesize that the inherent molecular mechanism responsible for the small, undersized mandible is overexpression of dual-specificity tyrosine (Y) phosphorylation regulated kinase 1A (*Dyrk1a),* a gene that is found in three copies in individuals with DS and Ts65Dn mice. To test our hypothesis, we bred Ts65Dn mice with *Dyrk1a* knockout mice, thus reducing *Dyrk1a* copy number to normal levels. This study provides the foundation for understanding the function of Dyrk1a. We also treated embryos with Epigallocatechin gallate (EGCG), a green tea polyphenol that is known to inhibit Dyrk1a activity. We will examine the molecular and cellular effects of Dyrk1a and EGCG on the developing PA1 on E9.5 embryos. In both the genetic and pharmacological manipulations, we expect to find a larger overall embryonic size, a larger PA1 size and increased number of NC cells.

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